49-61 have been added by this Amendment. A clean copy of the pending claims is included as **Exhibit A**.

I. Support for the Claims

Claims 50-61 find support in original claims 2-4, 14, and 15. Claim 49 finds support in original claim 1 and on page 19, lines 8-12 of the application. Claims 50-51 find support in original claim 1. No new matter is introduced by this amendment.

II. Support for the Amendment to the Specification

Incorrect statements made in the Application as originally filed have been corrected. Said corrections are supported by a Supplemental Declaration executed by all of the Inventors.

III. Response to Rejection Under 35 U.S.C. § 102(b)

Claims 43 and 44 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Nagase *et al.* (*DNA Res.*, 3:321-329, 1996) (hereinafter "Nagase"). Applicants respectfully traverse. Previously (Paper 10) the Examiner also rejected claims 1-4, 14, and 15 over Nagase. As claims 49-61 are based on original claims 1-4, 14, and 15 the substance of that rejection is also responded to by the instant Response.

As described in the Declaration of Dr. Brad Ozenberger, which accompanies this Response as Exhibit B, Nagase merely discloses and names a prediction of the primary structure of an unknown cDNA. Nagase did not put the public in possession of the instant invention. Nor does Nagase provide an enabling disclosure of the instant invention.

The cDNA clone designated KIAA0269, which is alleged to anticipate SEQ ID NO:1 of the present invention, is suggested by Nagase to be most closely homologous (29.9%) to an extensin-like protein from a species of corn. There is nothing in Nagase which suggests

any method of using the bare sequence prediction. In particular, there is nothing disclosed or described in Nagase suggesting that a nucleic acid molecule (SEQ ID NO:1) encoding a protein of SEQ ID NO:2 would bind Bcl-xL or modulate apoptosis in mammalian cells.

The claims of the instant invention are drawn to a nucleic acid molecule of SEQ ID NO:1, wherein the encoded protein is a Bcl-xL binding protein. There is no evidence provided by Nagase that would support the conclusion that the clone KIAA0269 encodes any useful molecule, especially not a Bcl-xL binding (pro-apoptotic) protein, and as such, Nagase cannot anticipate the claimed invention.

35 U.S.C. §102 (b) states that a person is entitled to a patent unless... (b) the invention was ... described in ...a printed publication in this or a foreign country...more than one year prior to the date of the application for patent in the United States.

The MPEP states at 2121.01:

> "In determining that quantum of prior art disclosure which is necessary to declare an applicant's invention `not novel' or `anticipated' within section 102, the stated test is whether a reference contains an `enabling disclosure'... ." *In re Hoeksema*, 399 F.2d 269, 158 USPQ 596 (CCPA 1968). A reference contains an "enabling disclosure" if the public was in possession of the claimed invention before the date of invention.

The MPEP goes on to explain the enablement requirement at 2164:

> The enablement requirement refers to the requirement of 35 U.S.C. 112, first paragraph that the specification describe how to make and how to use the invention. (emphasis added)

Simply stated, Nagase does not anticipate the instant invention because it does not disclose an enabling disclosure which includes how to use the invention. This conclusion is supported by analogous decisions which found a chemical to be novel where the alleged "prior art" failed to enable the "how to make" portion of the test. See for example, MPEP 2121.02 A which states:

> the mere naming of a compound in a reference, without more, cannot constitute a description of the compound
> ...

> When a prior art reference merely discloses the structure of the claimed compound, evidence showing that attempts to prepare that compound were unsuccessful before the date of invention will be adequate to show inoperability. *In re Wiggins*, 488 F.2d 538, 179 USPQ 421 (CCPA 1971).
> ...
> *In re Hoeksema*, 399 F.2d 269, 158 USPQ 596 (CCPA 1968) (A claim to a compound was rejected over a patent to De Boer which disclosed compounds similar in structure to those claimed (obvious homologs) and a process of making these compounds. Applicant responded with an affidavit by an expert named Wiley which stated that there was no indication in the De Boer patent that the process disclosed in De Boer could be used to produce the claimed compound and that he did not believe that the process disclosed in De Boer could be adapted to the production of the claimed compound. The court held that the facts stated in this affidavit were legally sufficient to overcome the rejection and that applicant need not show that all known processes are incapable of producing the claimed compound for this showing would be practically impossible.).(emphasis added)

Clearly, the Patent Office recognizes that the mere naming of a compound or providing its structure, as in Nagase, is not enough to anticipate a claimed compound.

Support for the patentability of the present invention is also found in the law and public policy of the "Written Description Requirement" in 35 U.S.C. §112, which the MPEP describes as:

> Another objective is to put the public in possession of what the applicant claims as the invention so that the public may ascertain if the patent applicant claims anything that is in common use, or already known. *Evans v. Eaton*, 20 U.S. (7 Wheat.) 356 (1822).

This view of the requirements for a proper description is also evident in the Revised Interim Utility Guidelines Training Materials wherein the Patent Office recognized that a lack of a disclosed utility gives rise to an enablement rejection under 35 U.S.C. § 112, first paragraph as well as under § 101. At page 10 of the Guidelines:

> **7.05.01** - UTILITY REJECTIONS UNDER 35 U.S.C. § 101 AND 35 U.S.C. 112, FIRST PARAGRAPH
> ...
> Claim [4] also rejected under 35 U.S.C. § 112, first paragraph.
> Specifically, since the claimed invention is not supported by either a [5] asserted utility or a well established utility for the reasons set forth above, one skilled in

> the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation. (emphasis added)

In fact, Example 3 of the Guidelines discloses a fact situation in which more disclosure is provided than that provided by Nagase and the Patent Office concludes that a §112 rejection is proper. Thus, in an analogous situation the Patent Office has recognized that a disclosure such as that provided in Nagase is not enabled; therefore Nagase cannot anticipate the instant invention.

Finally, one might argue that the use of Pablo to promote apoptosis is an inherent quality of the protein. Such an argument would be fallacious, however, as it confuses a disclosure of "how to use" an isolated nucleic acid molecule with a property of a nucleic acid. Use of the isolated nucleic acids of the instant invention to produce proteins which have a pro-apoptotic effect is not a property of the nucleic acids. Rather, production of proteins which have a pro-apoptotic effect is one use which can be made of the isolated nucleic acids.

Applicants therefore contend that Nagase does not anticipate the claimed invention and respectfully request withdrawal of the rejection of claims 43 and 44 under 35 U.S.C. § 102(b) and further request the pass to issue of all of the pending claims.

IV. Conclusion

It is the Applicants' belief that the pending claims are in condition for allowance, and action towards that effect is respectfully requested. If there are any matters which may be resolved or clarified through a telephone interview, the Examiner is requested to contact the undersigned attorney at the number indicated.

Gavin T. Bogle

Limited Recognition Certificate Attached

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Date: 3-12-02

EXHIBIT A

Claims

43. A recombinant expression vector comprising a polynucleotide encoding a Pablo polypeptide comprising the amino acid sequence of SEQ ID NO:2.

44. A genetically engineered host cell, transfected, transformed or infected with the vector of claim 43.

49. An isolated nucleic acid molecule comprising a nucleotide sequence encoding an isolated mammalian Bcl-xL binding protein, wherein said isolated mammalian Bcl-xL binding protein has 85% amino acid sequence identity with a Bcl-xL binding protein set forth in SEQ ID NO:2.

50. An isolated nucleic acid molecule comprising a nucleotide sequence encoding an isolated mammalian Bcl-xL binding protein, wherein said nucleotide sequence hybridizes to the complement of a nucleotide sequence set forth in SEQ ID NO:1 which encodes a Bcl-xL binding protein in 6X SSC at 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 50-65°C.

51. An isolated nucleic acid molecule comprising a nucleotide sequence encoding an isolated mammalian Bcl-xL binding protein as shown in SEQ ID NO:1.

52. A nucleic acid molecule comprising a nucleotide sequence encoding an isolated mammalian Bcl-xL binding domain, wherein said domain is a fragment of the nucleic acid molecule of claim 51.

53. The isolated nucleic acid molecule of claim 52 wherein the isolated Bcl-xL binding domain consists of amino acids 419-559 or amino acids 429-559 of SEQ ID NO:2.

54. The isolated nucleic acid molecule of claim 49, wherein said isolated mammalian Bcl-xL binding protein modulates apoptosis.

55. The isolated nucleic acid molecule of claim 50, wherein said isolated mammalian Bcl-xL binding protein modulates apoptosis.

56. The isolated nucleic acid molecule of claim 51, wherein said isolated mammalian Bcl-xL binding protein modulates apoptosis.

57. The isolated nucleic acid molecule of claim 49, wherein said nucleic acid molecule encodes a fusion protein.

58. The isolated nucleic acid molecule of claim 50, wherein said nucleic acid molecule encodes a fusion protein.

59. The isolated nucleic acid molecule of claim 51, wherein said nucleic acid molecule encodes a fusion protein.

60. A neural cell line stably expressing a heterologous Pablo polypeptide or an isolated Bcl-xL binding protein set forth in SEQ ID NO:2.

61. An isolated nucleic acid molecule comprising a heterologous nucleotide sequence encoding an isolated mammalian fusion protein having an amino acid sequence of SEQ ID NO:2, wherein the protein modulates apoptosis.